

Also of interest is the observation of Suda and Abe (1964) that the glaucoma-like scotomata produced by bulbar compression appear at lower intraocular pressures than in normal subjects. These observations do much to explain why simple tonometry and related tests have failed to provide an accurate index of the incidence of clinical glaucoma.

To summarize the present position, it has been established by population studies that simple glaucoma is a disease determined in the individual by a number of factors, the measurement of none of these being in itself sufficient to categorize the subject as normal or abnormal. As information from these studies accumulates, we are beginning to obtain more accurate estimates of the probability of the development of clinical glaucoma requiring treatment, but as yet our knowledge is insufficient to allow us to diagnose with confidence the patient in whom the premonitory signs indicate the inevitability of deteriorating visual function if treatment is not instituted.

There is, however, reasonable hope that such a goal is attainable, although the techniques involved may not be simple and will therefore be expensive—a fact of considerable relevance to the public health administrator who is approached for support in screening programmes.

COMMENTARY

OCULAR HYPERTENSION AND POPULATION SURVEYS

The concept of ocular hypertension is unhelpful and the intraocular pressure must always be correlated with the appearance of the discs. The highest intraocular pressure without field changes in the Cardiff survey was 34 and in the Bedford survey 29 mm.Hg. In the Bedford survey only two out of 138 persons with ocular hypertension (intraocular pressure 19 to 23 mm.Hg) developed field changes in a 5-year period, but two out of twelve with suspicious discs developed field changes in this time. Re-examination after 5 years of over 500 persons with normal tensions and normal discs revealed one case of raised tension with glaucomatous field defects. One of the major parameters is the change in pressure with time, about which very little is known.

In Armaly's population studies, four persons developed glaucoma during the follow-up period and three out of four of these would not have been spotted if the cut-off point had been 21 or 22 mm.Hg intraocular pressure. They were all in their twenties when the field defect was discovered and had other lesions which could have been spotted, such as abnormal blood sugar or vascular changes. The intraocular pressure levels in these four patients were by no means the highest in the population studied.

Some factors in the production of low tension glaucoma

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The enigma of low tension glaucoma has existed since von Graefe (1857a) described "amaurosis with excavation" which had all the ophthalmoscopic features of chronic simple glaucoma without elevation in intraocular pressure (Schnabel, 1908). It must be noted, however, that the intraocular pressure in his time was checked by digital tonometry. Von Graefe withdrew the concept, probably at the instigation of Donders, who believed

that all excavation of the optic nerve head was due to elevated intraocular pressure. The introduction of indentation tonometry by Schiötz (1905) established beyond any reasonable doubt the concept of optic nerve head excavation and atrophy without elevation in intraocular pressure. The pathology of both glaucoma and low tension glaucoma was found by Schnabel (1892, 1904a, b, 1905) to be a cavernous or lacunar atrophy of the optic nerve, and similar changes were investigated by Marie (1901) in the brain. It is now known that lacunar changes in the optic nerve and brain are due to disturbances of the circulation in small vessels (Fisher, 1965). Diurnal pressure variations were demonstrated to be responsible for some cases of low tension glaucoma in which the intraocular pressure was sometimes elevated when the patients were not under examination (Löhlein, 1926). Congenital malformations of the optic nerve head (Fuchs, 1928) and pressure on the optic nerve head from tumours of the pituitary and adjacent structures (Thiel, 1930) were shown to lead to excavation and atrophy of the nerve head. It was believed that calcification of the intracranial portion of the carotid artery pressing on the optic nerve (Knapp, 1932) was responsible for some cases of low tension glaucoma, but this change has been demonstrated in up to 50 per cent. of older people with no corresponding changes in the optic nerve head (Glees, 1936; Siegert, 1938). The association of calcified carotids with small degenerative changes in the small vessels feeding the optic nerve was suggested by many. Eyes with low coefficients of scleral rigidity (usually myopic eyes) were found to have higher intraocular pressures by applanation tonometry than by indentation tonometry (Winstanley, 1959), which accounted again for some patients with this anomaly. The introduction of tonography (Grant, 1950) saw the division of low tension glaucoma into those patients with normal outflow facilities and those with chronic simple glaucoma in whom the intraocular pressure was lowered by a diminution in aqueous production arising from compensatory or atrophic changes in the ciliary body.

Low tension glaucoma was found to be present in 0.15 per cent. of a total population study (Hollows and Graham, 1966b). Small arcuate scotomata were demonstrated in patients whose highest pressures were always below 20 mm.Hg (Armaly, 1966b), but the prevalence of the field changes was found to be greater in those patients with pressures over 20 mm.Hg. These findings showed that factors other than intraocular pressure must be incriminated in the production of visual field changes in the arcuate area. After the steroid provocative test was introduced it appeared that 40 per cent. of patients with low tension glaucoma responded with a high rise in intraocular pressure (Armaly, 1967a).

Reduced resistance of the optic nerve to intraocular pressure due to systemic factors was suggested by Haas (1962), and the presence of a low perfusion pressure or a history of transient but severe hypotensive episodes in patients with low tension glaucoma was commented on by Johnson and Drance (1968). Harrington (1959) suggested that low tension glaucoma was due to a decreased blood flow, which was produced by arteriolar sclerosis and partial occlusion of the optic nerve vessels.

The animal experiments of Hayreh (1970) verified that imbalance between intraocular pressure and systemic blood pressure altered the perfusion of the ciliary circulation and the circulation in the nerve head.

In defining low tension glaucoma, many features have been introduced or excluded by the various authors, and although all of them used the same label of low tension glaucoma, the conditions which were actually studied were often entirely different.

The present study was started in order to try to establish the interaction of multiple factors in the production of this disease process.

Method of present study

To study the factors producing low tension glaucoma, patients were selected in whom the optic nerve head was undoubtedly excavated and atrophic, and in whom there was an accompanying classical visual field defect indicating involvement of nerve fibre bundles. Only those with obviously unrelated causes responsible for the defects, such as tumours and malformations of the disc, were excluded. Cases of spurious low tension, in which the intraocular pressure was elevated on a diurnal basis or was due to low coefficients of scleral rigidity, were also weeded out. The patients were investigated from the medical and ocular points of view.

In order to select undoubted patients with low tension glaucoma and in spite of remarks about "normal" intraocular pressure levels in older people, only those persons whose highest applanation intraocular pressures around the clock in the affected eyes were 21 mm.Hg or less, were chosen for further study and analysis. All had field defects of the classical glaucoma type with very dense and reproducible nerve fibre bundles, scotomata shown by static and kinetic perimetry on the ocular perimeter. The angles of the anterior chambers were wide open with no signs of present or previous uveitis or other ocular disease. All patients with a previous history of retrobulbar neuritis, trauma, or angle-closure glaucoma were excluded. None of them had had glaucoma surgery or were receiving therapy at the time of the evaluation. No lens extractions had been undertaken in any of the cases studied.

Besides a standard ocular examination, almost all patients had tonography and diurnal tension studies at 6, 9, and 11 a.m., and 2, 5, and 10 p.m. Ophthalmodynamometry, utilizing calibrated dynamometers, was carried out according to the technique described by Weigelin and Lobstein (1963). A vascular neurologist evaluated all patients. X-ray examinations of the chest, skull, and optic foramina, electrocardiography, blood profiles and erythrocyte sedimentation rate, fasting and 2-hour post-prandial blood sugars, venereal disease research laboratory tests, blood urea nitrogen, cholesterol, and protein-bound iodine or its equivalent were carried out. Most patients had blood coagulation studies, including the euglobulin lysis time and platelet adhesiveness. A steroid provocative test, using 0.1 per cent. dexamethasone three times daily into one eye for 4 weeks, was carried out where feasible. Previous medical and hospital records were available for scrutiny. Six patients (10 eyes), whose intraocular pressure reached a peak above 21 mm.Hg on the diurnal tension curve, were excluded from the study even though they had been diagnosed as cases of low tension glaucoma on repeated daytime tonometric readings.

Patients were matched with ocular hypertensives of the same age and sex whose intraocular pressure was above 21 mm.Hg but whose discs and fields were completely normal. The matched "controls" underwent exactly the same sequence of ocular, neurovascular, and laboratory evaluations. They came from a private referral facility and a veterans glaucoma clinic.

The two groups were compared with one another with regard to haemodynamic crises, vascular disease, blood pressure, ophthalmic artery pressure, and diabetes. A marginal χ^2 test was employed to determine the statistical separation of the two groups with regard to these parameters.

Some of the patients were seen only once for a complete consultation, which included the above procedures, but most of them were followed for from 1 to 7 years with serial examinations of the visual fields, optic nerve head, intraocular pressure, ocular dynamics, blood coagulation, and any other tests deemed necessary for the study of their clinical progress.

Results

29 patients (41 eyes) fulfilled the criteria of low tension glaucoma as defined. Twelve of these had bilateral low tension glaucoma, twelve others had an undamaged fellow eye, and five had a severely damaged fellow eye with intraocular pressures above 21 mm.Hg (*i.e.* classical chronic simple glaucoma).

Eighteen of the 29 patients were men and eleven women. Their ages ranged from 44 to 83 years, but the age distribution (Fig. 1, overleaf) showed a great preponderance of older individuals, 76 per cent. being 60 years of age or older.

The coefficients of outflow facilities (Fig. 2) showed that over half of the low tension glaucoma eyes had an excellent outflow facility >0.20 and therefore a Po/C of 100 or less. Sixteen of the 19 patients were tested for steroid responsiveness, and only three showed the strongly positive response of the PhPh type; 2 others showed an intermediate response of the PhPl type, whereas the remaining eleven had a minimal pressure response of less than 5 mm.Hg (PIPl). Two of the three high responders had a normal outflow facility and a low Po/C ratio.

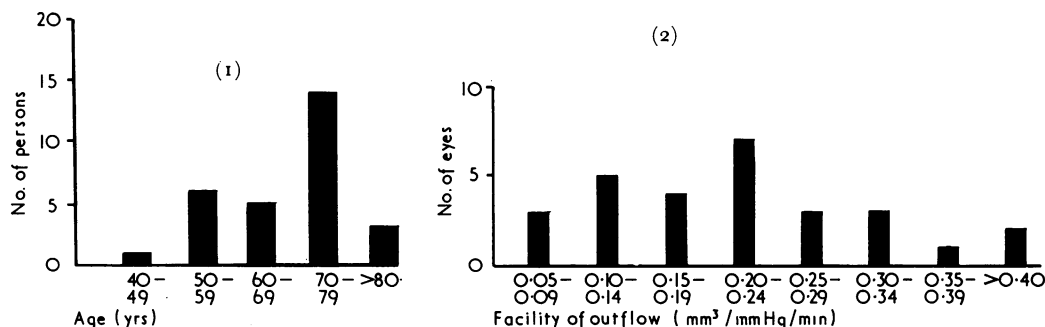


FIG. 1 Age distribution of 29 patients with low tension glaucoma, showing the preponderance of older age groups

FIG. 2 Distribution of outflow facilities of 41 low tension glaucoma eyes

In the majority of the eyes tested the highest recorded intraocular pressures were in the high teens or at the 20 mm.Hg level (Fig. 3). The highest pressures were often found on a diurnal tension curve, and the repeated day-time applanations were usually even lower.

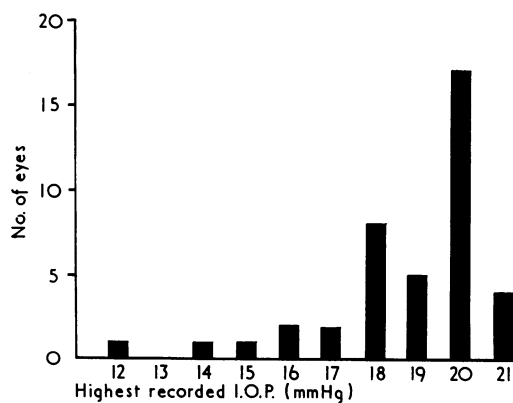


FIG. 3 Level of highest intraocular pressure of 41 eyes with low tension glaucoma obtained on diurnal pressure studies

Profiles of the twelve patients who had uniocular damage with a normal fellow eye appear in Table I. None of the damaged eyes had an intraocular pressure more than 2 mm.Hg higher than its undamaged fellow eye. Three of the twelve patients showed a poorer outflow facility on the affected side with a more elevated Po/C ratio. Three other patients showed a discrepancy between the ophthalmic artery pressures of the two sides, the damaged eye having the lower pressure. Two of those with the ophthalmic artery pressure discrepancy had also had a haemodynamic crisis, during which the differences between the two ophthalmic artery pressures may have been more important or even crucial to the perfusion of the corresponding nerve. In two of the three patients in whom there was

Table I Profiles of the two eyes in patients with uniocular low tension glaucoma

Case no.	Eye	Highest IOP (mm.Hg)	“C”	Po/C	Ophthalmic pressure (mm.Hg)		Blood pressure (mm.Hg)	Haemodynamic	Clinical vascular disease
					Systolic	Diastolic			
1	Damaged	20	0.13	100		103	210/130	Yes	
	Fellow	20	0.09	167		103			
2	Damaged	20	0.24	50	147	68	120/75		
	Fellow	20	0.22	55	103	50			
3	Damaged	18	0.29	52	126	61	125/75		Suspect right carotid
	Fellow	20	0.21	76	131	63			
4	Fellow	19	0.16	94	138	41	125/60		
	Damaged	20	0.12	133	146	41			
5	Fellow	18	0.38	47	157	74	170/85		
	Damaged	19	0.36	47	160	73			
6	Damaged	12	0.18	72	92	32	145/80		
	Fellow	22	0.18	0.117	123	52			
7	Fellow	23	0.20	95	111	50	125/75		Suspect left carotid
	Damaged	21	0.16	125	103	50			
8	Damaged	20	0.32	50	100	53	140/90	Yes	
	Fellow	19	0.37	41	120	52			
9	Damaged	20	—	—	102	54	125/75	Yes	
	Fellow	198	—	—	109	48			
10	Damaged	18	—	—	115	47	140/85	Yes	Right carotid
	Fellow	22	—	—	135	58			
11	Damaged	19	0.34	44	115	50	120/70		
	Fellow	21	0.29	41	114	53			
12	Damaged	16	0.28	55	154	86	165/100		Vascular occlusion right lower retinal artery
	Fellow	15	0.29	52	154	85			

asymmetry of the coefficients of outflow facility, haemodynamic crises had also occurred and may have been important, for if the intraocular pressure in the eye with the poorer outflow facility was very slightly higher at the time of the crisis than that in the fellow eye, this might have added to any perfusion difficulties during the crisis. Yet another patient had a clinical suspicion of carotid artery involvement of the side of the eye with low tension glaucoma, even though no ophthalmic artery pressure discrepancy was ophthalmodynamometrically recorded; finally, a local vascular occlusion of a retinal arterial vessel on the optic nerve head accounted for the one-sidedness of the damage in yet another patient. Eight out of the twelve patients with uniocular low tension glaucoma therefore had a suggestive cause for their asymmetry and half of them had a haemodynamic crisis in addition to that. Three of the remaining four in whom no apparent reason for asymmetry was established had a very low systemic blood pressure for their age, but the significance of this is not immediately apparent. The discs of the normal fellow eyes showed a much larger cup:disc ratio than that reported in normal populations. There was an asymmetry in the cup sizes in all of the patients with uniocular involvement (Fig. 4, overleaf).

The central vision was good in the great majority of the 41 eyes (Fig. 5, overleaf), and most of the patients were discovered on routine ocular examination or refraction. The few eyes with a poor visual acuity had cataracts, macular disease, or small vessel occlusion to account for it. The excellence of the vision and the lack of symptoms is an important feature, because, in spite of the major pathology at the optic nerve head, unless entire populations are screened, the number of cases of low tension glaucoma diagnosed will represent only a portion of the cases existing in the population.

Ten of the 29 patients had a well-documented haemodynamic crisis with a major fall in blood pressure before the routine discovery of symptomless disc and field changes. These crises were mostly gastrointestinal or uterine haemorrhages, but a cardiac arrest and very severe hypotension during anaesthesia were also recorded. In addition to the ten severe crises, four other patients had minor haemodynamic upsets associated with symptomatic postural hypotension, congestive cardiac failure, or intermittent cardiac arrhythmia.

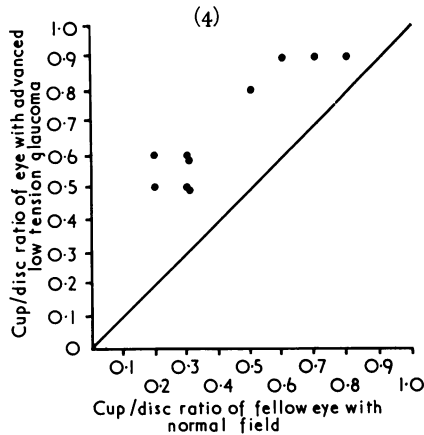


FIG. 4 Cup ratios of uniocular low tension glaucomas. The damaged eyes had large cups but many of the uninvolved fellow eyes also showed large cups

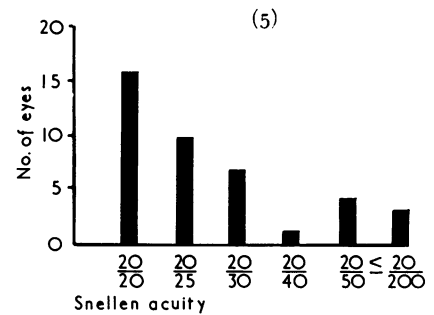


FIG. 5 Distribution of visual acuities of 41 low tension glaucoma eyes

In some of the fourteen patients with major and minor crises (Table II), other anomalies apart from the haemodynamic upsets were also present. A comparison between the haemodynamic crisis of a low tension glaucoma group and of ocular hypertensives matched for age and sex showed the difference between them to be highly significant at the 1 per cent. level of confidence. The presence of a hypercoagulopathy in eight of the fourteen patients with crises should be noted as it may be of significance.

Table II Distribution of other abnormalities in low tension glaucoma patients with haemodynamic crisis

Low blood pressure	Vascular disease	Diabetes	Hyper-coagulation	Ophthalmic artery pressure deficiency	Progress of visual field loss
—	—	×	×	×	No
—	—	—	×	—	No
—	—	—	—	—	No
—	×	—	—	—	No
×	×	—	Not tested	—	No
—	—	—	×	—	No
—	×	—	×	—	Not followed
—	—	—	—	—	No
×	×	×	—	—	No
—	—	—	×	—	No
—	—	—	×	—	Yes
×	—	—	×	—	Not followed
—	—	—	×	×	Not followed
—	×	—	—	—	No

Nine of the 29 patients had a low systemic blood pressure (Figs 6 and 7) of 120 mm.Hg or less systolic and/or 80 mm.Hg or less diastolic. In addition, three others had borderline blood pressures, the mean ophthalmic artery blood pressure readings being 10 mm.Hg less than that expected from their systemic blood pressure levels. The perfusion pressure of the optic nerve head may be as significantly influenced by such deficits as by low systemic

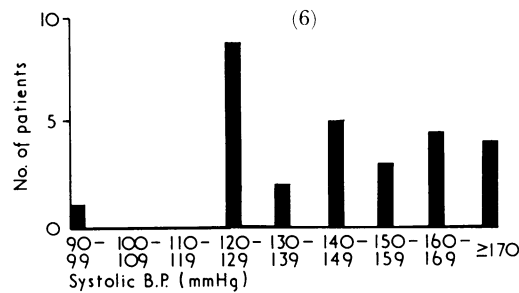


FIG. 6 Distribution of systolic blood pressure of 29 patients with low tension glaucoma

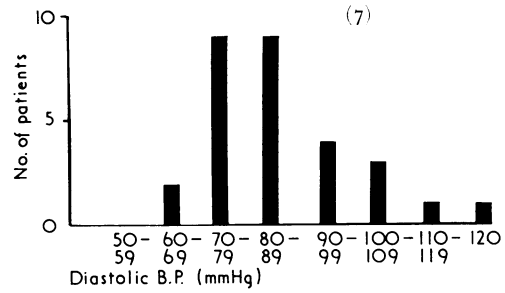


FIG. 7 Distribution of diastolic blood pressure of 29 patients with low tension glaucoma

blood pressure. A statistical comparison of a low tension glaucoma group with their matched ocular hypertensive counterparts shows the groups to be statistically dissimilar with regard to systolic blood pressure ≥ 120 mm.Hg (5 per cent. level of confidence), diastolic blood pressure ≥ 70 mm.Hg (1 per cent. level of confidence), and mean blood pressure ≥ 110 mm.Hg (1 per cent. level of confidence). The systemic features associated with the low blood pressure are listed in Table III. The ophthalmic systolic artery and ophthalmic diastolic blood pressures of the group were also low (Figs 8 and 9).

Table III Distribution of other abnormalities in low tension glaucoma patients with low blood pressure

Vascular disease	Hyper-coagulation	Diabetes	Haemodynamic crisis	Ophthalmic artery pressure deficiency	Progression of visual field loss
—	—	—	—	×	Yes
—	—	—	—	—	Yes
—	×	—	—	—	Yes
×	—	×	×	—	No
—	—	—	—	—	Yes
×	Not tested	—	×	—	No
×	×	—	—	—	No
—	×	—	×	×	Not followed
—	—	—	—	—	No

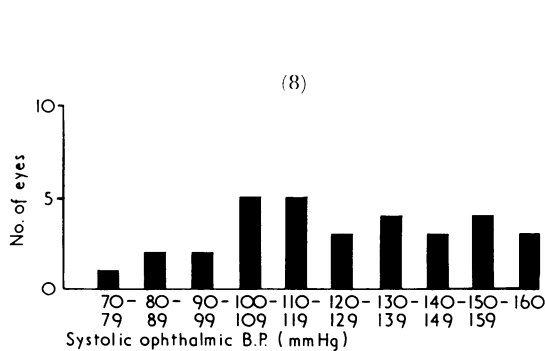


FIG. 8 Distribution of systolic ophthalmic pressure of 29 patients with low tension glaucoma

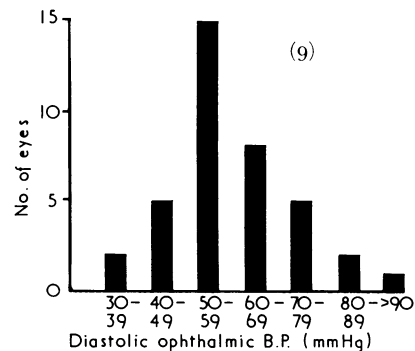


FIG. 9 Distribution of diastolic ophthalmic pressures of 29 patients with low tension glaucoma

Seven of the 29 patients had clinically overt vascular disease. Cardiovascular disease accounted for some, while others had evidence of lacunar infarction in the nervous system, or disease in the carotid or vertebrobasilar vessels. In addition, four others had clinical suspicion of carotid disease which was symptom-free and was not angiographically evaluated. It is of interest that seven of the eleven patients with overt vascular disease, in whom coagulation studies were available, showed a hypercoagulable state (Table IV), and five out of the eleven had a haemodynamic crisis which might have made the vascular pathology more significant.

Table IV *Distribution of other abnormalities in low tension glaucoma patients with overt vascular disease*

<i>Low blood pressure</i>	<i>Ophthalmic artery pressure deficiency</i>	<i>Diabetes</i>	<i>Hyper-coagulation</i>	<i>Haemodynamic crisis</i>	<i>Progression of visual field loss</i>
—	—	—	—	×	No
×	—	—	Not tested	×	No
—	×	×	×	—	Yes
—	—	—	—	×	Yes
—	—	×	×	—	Yes
—	—	—	×	×	Not followed
—	—	—	×	—	Yes
×	—	×	—	×	No
×	—	—	×	—	No
—	—	—	—	×	No
—	—	—	×	—	No

Five of the 29 patients were clinically diabetic. Most of these had known this before being examined. As expected, most had associated systemic findings (Table V). Two of the diabetics had a family history of glaucoma, which is not shown in the Table. The low tension glaucoma group had more overt vascular disease and diabetes than their ocular hypertensive counterparts, but these differences were not statistically significant.

Table V *Distribution of other abnormalities in low tension glaucoma patients with diabetes*

<i>Vascular disease</i>	<i>Hyper-coagulation</i>	<i>Low blood pressure</i>	<i>Ophthalmic artery pressure deficiency</i>	<i>Haemodynamic crisis</i>	<i>Progression of visual field loss</i>
—	×	—	×	×	No
×	×	—	×	—	Yes
×	×	—	—	—	Yes
—	Not tested	—	—	—	Not followed
×	—	×	—	×	No

Coagulation studies were carried out in 26 of the 29 patients and only ten of these were entirely normal, while sixteen had either increased platelet adhesiveness (over 60 per cent. adhesiveness) or an abnormal euglobulin lysis time (longer than 6 hours). These findings suggest a greater tendency to thrombosis as a result of interference with the fibrinolytic system. Such disturbances have been found in association with myocardial infarction and cerebrovascular disease (Lancet, *Editorial*, 1968). The finding of such an anomaly in patients with low tension glaucoma cannot—at this time—be accurately evaluated, but it suggests vascular disease and was present in eight out of fourteen patients in whom a

major haemodynamic crisis occurred, and in six out of ten patients with overt extraocular vascular disease. It may be that, when there is hypercoagulation—usually associated with small vessel disease, the addition of a haemodynamic crisis may produce perfusion difficulties more readily and this may produce infarction of the optic nerve head. The platelet adhesiveness and euglobulin lysis time of the 29 low tension glaucoma patients (Figs 10 and 11) were compared with those obtained in a group of cataract patients in whom glaucoma was excluded. There was a higher percentage of abnormality in the platelet adhesiveness and prolonged euglobulin lysis time among the low tension glaucoma patients. Most of the cataract patients who showed hypercoagulability had overt vascular disease.

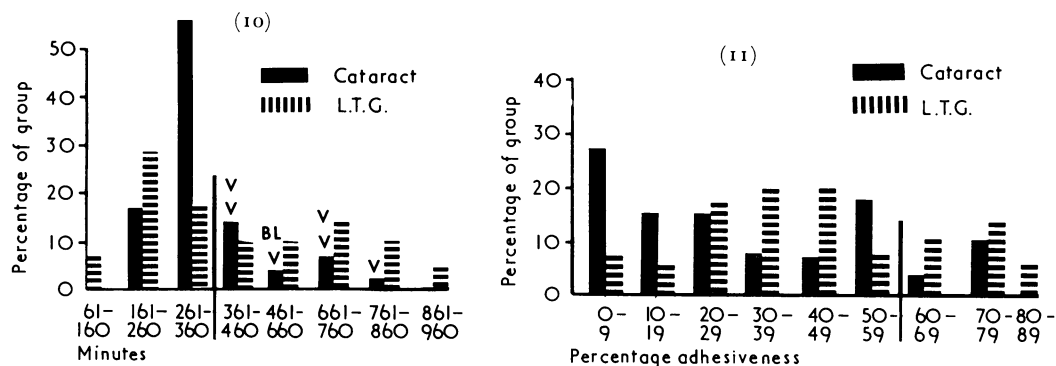


FIG. 10 Distribution of euglobulin lysis times of low tension glaucoma group compared with a group of cataract patients. The vertical line indicates upper limit of "normality" accepted by laboratory. Vascular disease among cataract patients is marked by a V

FIG. 11 Distribution of the percentage platelet adhesiveness of low tension glaucoma group and a group of cataract patients. Vertical line denotes upper level of "normality" accepted by laboratory

In six of the 29 low tension glaucoma patients, small linear sector disc haemorrhages were observed at the optic nerve head (Fig. 12, overleaf). In some of these, the haemorrhages occurred in areas which had already been severely damaged. In a previous report, the appearance of these haemorrhages was associated with fresh field defects and was thought to be a sign of vascular insufficiency at the nervehead (Drance and Begg, 1970). The frequency of the occurrence of transient disc haemorrhages in this group of patients, many of whom were seen only once in consultation, must be commented on. All of them also had other systemic features (Table VI, overleaf) which might be of significance.

Radiological calcification of the internal carotids was recorded in six of the 29 patients.

Five of the 29 patients were highly myopic, and three patients out of the whole group had a family history of glaucoma.

Considering only haemodynamic crises, low blood pressure, overt vascular disease, diabetes, and hypercoagulable states, there were only two patients in the entire group of 29 cases of low tension glaucoma, who had no abnormality apart from the abnormal optic nerve head with field defect, and eight others in whom there was only one of the other abnormalities (2 severe haemodynamic crisis, 4 low blood pressure, 1 diabetes, and 1 coagulopathy). The remaining nineteen patients (65 per cent.) showed more than one other pathological factor and some as many as three or more. Two of the eight who had only one other abnormality were also highly myopic, which may have been a contributory factor.

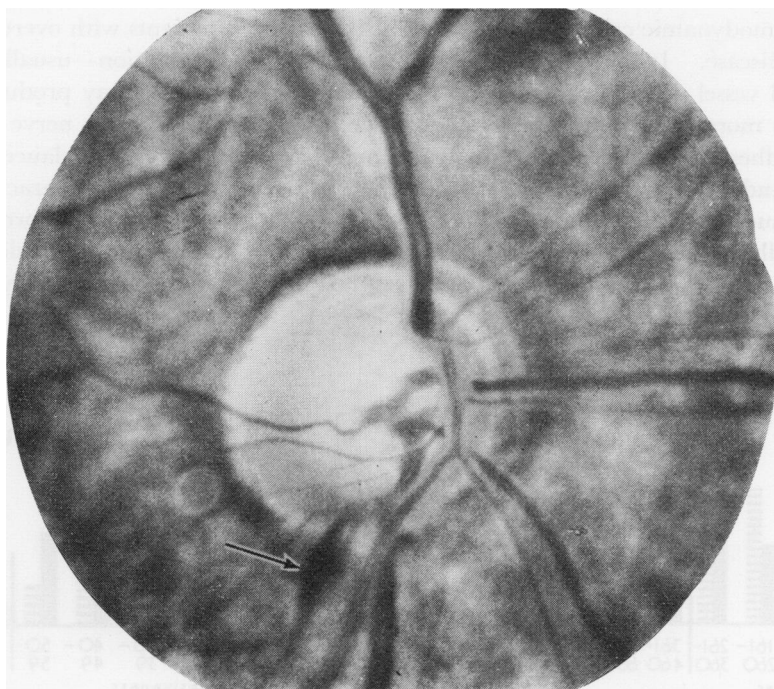


FIG. 12 Optic nerve head of a patient with low tension glaucoma, showing linear haemorrhage of optic disc (arrow)

Table VI *Distribution of other abnormalities in low tension glaucoma patients with disc haemorrhages*

<i>Vascular disease</i>	<i>Hyper-coagulation</i>	<i>Low blood pressure</i>	<i>Diabetes</i>	<i>Ophthalmic artery pressure deficiency</i>	<i>Haemodynamic crisis</i>	<i>Progression of visual field loss</i>
—	×	—	—	—	×	No
×	—	—	—	—	—	Yes
—	—	—	—	—	×	No
×	×	×	—	—	—	No
—	×	—	—	—	×	Yes
—	×	×	—	×	×	Not followed

Progression of field defects

Of the 29 patients studied, 24 were followed with repeated plotting of the visual fields for periods varying from 1 to 7 years, and in most instances there were at least two follow-up field profiles and sometimes as many as fifteen (Table VII). Fourteen of the 24 patients showed no progression of field defects, but in ten the fields deteriorated. In the eleven patients who had a major haemodynamic crisis, ten of the eleven—who were followed—showed no change in the visual field and only one showed some progression. The patients with other abnormalities, such as low blood pressure, overt evidence of vascular disease, or diabetes, who had a haemodynamic crisis, showed no progression. Four out of the six

Table VII *Distribution of factors found in low tension glaucoma patients, according to progression of visual field loss*

<i>Visual field defect</i>	<i>Haemodynamic crisis</i>	<i>Low blood pressure</i>	<i>Ophthalmic artery pressure deficiency</i>	<i>Myopia</i>	<i>Hyper-coagulation</i>	<i>Family history</i>	<i>Vascular disease</i>	<i>Diabetes</i>
Progression	—	×	×	—	—	—	—	—
	—	×	—	—	—	—	—	—
	—	—	—	×	×	—	—	—
	—	×	—	×	×	—	—	—
	—	×	—	×	—	—	—	—
	—	—	×	—	×	—	×	×
	—	—	—	—	×	—	×	—
	—	—	—	—	×	—	×	×
	—	—	—	—	×	—	×	—
	×	—	—	—	×	—	—	—
No change	×	×	—	—	—	—	×	—
	×	—	—	—	—	—	×	—
	×	—	×	—	×	—	—	×
	×	—	—	—	×	—	—	—
	×	—	—	—	—	—	×	—
	×	—	—	—	×	—	—	—
	×	—	—	—	—	—	—	—
	×	×	—	—	—	—	×	×
	×	—	—	—	×	—	—	—
	—	×	—	—	×	—	×	—
	—	×	—	—	×	—	×	—
	—	—	—	—	×	—	—	—
	—	—	—	—	×	—	×	—

patients who had a low blood pressure and who did not have a haemodynamic crisis showed progression of their disease, while the four who had a crisis remained without change. Four of six patients with overt vascular disease who were followed and who did not have a haemodynamic crisis showed progression of visual field defects whereas four who had a crisis remained unchanged. The two diabetics who had a haemodynamic crisis showed no progression, but in the two who had no crisis the visual fields deteriorated in subsequent years.

Discussion

In this series, 93 per cent. of the patients with low tension glaucoma showed systemic abnormalities, and haemodynamic crises and low blood pressures occurred statistically significantly more frequently in them than in undamaged ocular hypertensives matched for age and sex. Patients and controls did not differ significantly in frequency of diabetes, high myopia, overt extraocular vascular disease, and family history. It is possible that ocular hypertensives may be protected against haemodynamic crises, but this has not been tested and will have to await further study. The tests for hypercoagulability have not yet been carried out in the ocular hypertensive controls.

The present study shows a very significant association of haemodynamic crises with excavation, atrophy, and nerve fibre bundle defects, yet it is known that such crises produce the clinical picture only in the elderly and practically never in the young. One must wonder, therefore, about an association of small or large vessel changes which occur in the

elderly and practically never in the young. As damage sometimes occurs in only one eye after a crisis, there must be reasons for such asymmetry. These may be a slightly higher intraocular pressure on the damaged side or a partial stenosis of the carotid artery, or maybe even local changes in the small vessels feeding one nerve head which cannot be recognized clinically. These factors were suggested by the findings previously reported (Drance, Wheeler, and Pattullo, 1968).

A low systemic blood pressure was also found to be significantly more common in subjects with low tension glaucoma than in undamaged ocular hypertensives. The blood supply of the optic nerve head is favourably influenced by an adequate perfusion pressure (ophthalmic artery pressure less the intraocular pressure), and adversely by local vascular disease. The blood supply of the nerve in a person with a low blood pressure, particularly if there is in addition a partial stenosis of the carotid, ophthalmic, or one of the posterior ciliary arteries, may be susceptible to small changes in intraocular pressure, which—while still statistically “normal” for a population—may be twice as high as the intraocular pressure which prevailed in the same individual when he was younger. The different effects on perfusion of the optic nerve of a genetically-determined low blood pressure and a low blood pressure produced by failure of the cardiac pump must receive attention.

Abnormalities in the coagulation-fibrinolytic system were found in 61 per cent. of the group and have been shown to be associated with vessel disease. This abnormality may, like diabetes, point to a disturbance of the small vessels of the optic nerve head, making the circulation precarious when the intraocular pressure is raised or the blood pressure is low. As uncomplicated carotid disease is only rarely accompanied by optic atrophy, the involvement of small vessels is probably a more important factor, and when it is present even small changes in ophthalmic pressure—normally well tolerated—may produce damage to the nerve.

The finding of small haemorrhages on six optic discs in the 29 patients, even though these were transient phenomena and easily missed, has already been commented on. Such haemorrhages always accompany ischaemic optic neuropathy (Foulds, 1969). In patients commonly seen with ischaemic optic neuropathy, the infarction is usually total or subtotal, and the patients present themselves because of central visual loss or the detection of a dense arcuate sector-shaped, or more often altitudinal, field loss. The patients with glaucoma or low tension glaucoma, on the other hand, in whom we have noted these haemorrhages, had no complaints; their vision was well maintained and the events were observed only because of the repeated routine ophthalmoscopy which was undertaken as a follow-up for their glaucoma or low tension glaucoma. In both conditions, the haemorrhages probably indicate small episodes of infarction or vascular insufficiency to optic nerve tissue. After such haemorrhages, notching of the involved neuroretinal rim has been described (Begg, Drance, and Sweeney, 1971) and has occurred some 2 to 3 months after the haemorrhage has disappeared. The optic nerve after the usual ischaemic neuropathy becomes atrophic but rarely cupped.

This raises the important question of the reason for the additional presence of cupping and excavation which accompanies optic atrophy in the glaucomas and low tension glaucomas as opposed to its absence in ischaemic neuropathy. The possible reasons that have been suggested are:

- (1) The pre-existence of cupping, as a congenital or familial feature, before the development of atrophy.

(2) The enlargement of the cups in some patients at an earlier stage of the disease when their intraocular pressures were much higher. There would be patients with the so-called "cured burnt-out glaucoma".

(3) The production of large cups as a result of the vascular insufficiency which produces the infarction and atrophy.

The existence of large cups in normal people and their families is well known, but their frequency is not very great in Caucasian populations (Armaly, 1967c). The acquired enlargement of the optic cup in cases of congenital glaucoma and in young individuals with high intraocular pressure was well documented (Shaffer and Hetherington, 1969). It could be argued that our patients all present burnt-out high pressure glaucoma, but this is most unlikely to apply to all of them, as 50 per cent. had remarkably normal outflow facilities in addition to their low intraocular pressure, and two-thirds of those tested had a low steroid response. There are likely, therefore, to be relatively few patients in this series who have gone through a high pressure phase. The large size of the optic cups in the normal fellow eyes of patients with uniocular-tension glaucoma suggests that pressure elevation was not the major reason for their large cups.

Schnabel found that, as fresh notches of the neuroretinal rim developed, they coalesced and involved the neuroretinal tissue to the disc margin. He also described a haemorrhage on the disc of one of his patients which was followed by excavation. The development of excavation in low tension glaucoma was always slow, whereas such notches occurred as early as 10 to 12 days after acute attacks of glaucoma. We have also seen slow disc changes after a small disc haemorrhage (Begg and others, 1971).

High myopia must also be considered as a factor which could influence the susceptibility of the nerve head to small intraocular pressure changes or other adverse factors of perfusion.

There are probably many mechanisms by which an optic nerve head may become cupped and atrophic. At least two ways have actually been observed by us in this group of patients. One had a pre-existing large cup which was followed by atrophy of a segment of the neuroretinal rim after a local vascular occlusion; the other developed notching of the neuroretinal rim after the appearance of a small haemorrhage on the disc with the appearance of a corresponding nerve fibre bundle defect considered to be a small optic nerve infarction. A third mechanism could be inferred, though it was not witnessed, in an old man with deep cupping of both discs who developed optic atrophy of one disc after massive gastrointestinal bleeding. The presence of cupping in an atrophic disc does not necessarily differentiate an acute from a chronic vascular impairment (Hayreh, 1970).

Low tension glaucoma does not always progress, in fact in 58 per cent. of the patients followed the visual field defects did not progress. The lack of progression of the field defects in almost all the patients who had a haemodynamic crisis (99 per cent.) and the progression in those who did not have such a crisis (70 per cent.) is an important finding and can be valuable in estimating prognosis. A patient in whom a haemodynamic crisis precedes the discovery of low tension glaucoma is unlikely to show deterioration in his visual field defects unless he has another crisis. The presence of low blood pressure, vascular disease, high myopia, and diabetes in the absence of such a crisis, makes slow progression of the field defects likely.

I would suggest that in low tension glaucoma we have an ischaemic process of the optic nerve head which may be the result of many interacting factors. The search for a single cause or process which leads to this condition may therefore continue to be frustrating. Even the separation of low tension glaucoma from glaucoma proper is artificial and lacks

significance. It seems absurd to think of two separate diseases occurring in those patients with classical low tension glaucoma in one eye and overt glaucoma in the other. It seems unreasonable to find family histories of classical open-angle glaucoma (with high pressures) in patients showing typical low tension glaucoma unless a single disease is involved. It seems unreasonable to label a patient as having glaucoma when he has had low tension glaucoma for years, just because he later develops a small rise in intraocular pressure or an "abnormal" outflow facility. Chronic simple glaucoma and low tension glaucoma are much more likely to be manifestations of a disease process in which many factors assume varying importance in interfering with perfusion of the optic nerve head.

A clearer recognition and understanding of the factors concerned in producing low tension glaucoma—some of which have been identified—and the significance of intraocular pressure as an important but by no means the only factor leading to ischaemia of the optic nerve head, may help to answer some of the enigmas of chronic simple glaucoma itself.

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COMMENTARY

TREATMENT OF LOW TENSION GLAUCOMA

A patient who presents with infarction of the optic nerve head without a preceding shock-like state should have everything done that is possible medically to try and reduce the intraocular pressure in the hope of manipulating the only factor that can be manipulated ophthalmologically. It is equally important for the cardiologists and physicians to treat the patients for other abnormalities, such as congestive cardiac failure, anaemia, and arrhythmias, in order to make the perfusion of the optic nerve head efficient. The use of strong miotics and long-acting Diamox is indicated in this condition and on occasions even surgery may be indicated for further reduction in intraocular pressure.

Open-angle glaucoma

HANS GOLDMANN

Berne

Statistics of the distribution of eye tension do not permit us to distinguish between normal and pathological pressure. Mathematical statistics represent a distribution of discrete values by a smooth continuous curve going on to infinity. Every point of this curve has a defined probability and only this probability distinguishes the different abscissae of the curve. 15 mm.Hg is a frequent, 40 mm.Hg a rare ocular tension. Mathematically—that is all. Nothing is said about normal or pathological. Only the connection between intraocular pressure distribution and visual field decay allows a distinction between the probable normal and the probable pathological. Not because 26 mm. is rare in the general pressure distribution curve, but because many patients with long-standing pressure around